

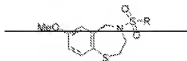
AMENDMENT

In the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.
 Before examination on the merits, please amend the claims as follows:

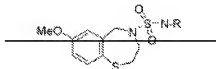
1-12. (Cancel)

13. (Currently Amended) A method for increasing binding of FKBP12.6 to RyR2 in a subject, or limiting or preventing a decrease in the level of RyR2-bound FKBP12.6 in a subject, comprising administering an effective amount of an agent to the subject, ~~in an amount effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the subject,~~ wherein the agent is selected from the group consisting of described by the formula:



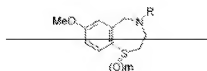
—(a)

wherein R = aryl, alkenyl, alkyl, $(CH_2)_nNR'_1$, or $(CH_2)_nSR'_1$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



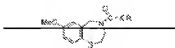
—(b)

wherein R = aryl, alkyl, $(CH_2)_nNR'_1$, or $(CH_2)_nSR'_1$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



—(e)

wherein $R = CO(CH_2)_n, XR'_{25}, SO_2(CH_2)_n, XR'_{25}$ or $SO_2NH(CH_2)_n, XR'_{25}$, and $X = N$ or S , and $n = 1, 2$, or 3 , and $R' =$ alkyl or cycloalkyl; and wherein $m = 1$ or 2 ;



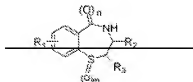
—(d)

wherein $R =$ aryl, alkyl, $(CH_2)_n, NR'_{25}, (CH_2)_m, SR'_{25}$, and $n = 0, 1, 2$, or 3 , and $R' =$ alkyl or cycloalkyl; and wherein $X = NH$ or O ;



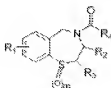
—(e)

wherein $R_1 = OR', SR', NR',$ alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and $R' =$ alkyl, aryl, or H; wherein $R_2 = H$, alkyl, or aryl; and wherein $R_3 = H$, alkyl, or aryl;



—(f)

wherein $R_1 = H, OR', SR', NR',$ alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and $R' =$ alkyl, aryl, or acyl; wherein $R_2 = H$, alkyl, alkenyl, or aryl; wherein $R_3 = H$, alkyl, alkenyl, or aryl; wherein $m = 0, 1$, or 2 ; and wherein $n = 0$ or 1 ;



(g)

wherein R₁ = H, OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R'
= alkyl, aryl, or acyl; wherein R₂ = H, alkyl, alkenyl, or aryl; wherein R₃ = H, alkyl, alkenyl, or
aryl; wherein R₄ = H, halide, alkenyl, carboxylic acid, or an alkyl containing 0, S, or N; and
wherein m = 0, 1, or 2; and

~~(h) any or is an~~ oxidized form thereof.

14. (Cancel)

15. (Original) The method of claim 13, wherein the subject is a human.

16. (Cancel)

17. (Currently Amended) The method of claim 13, wherein the subject has, or is a
candidate for, a cardiac ~~arrhythmia, heart failure, and/or exercise-induced sudden cardiac death~~
condition selected from the group consisting of cardiac arrhythmia, tachycardia, atrial
arrhythmia, atrial tachyarrhythmia, atrial fibrillation, sustained atrial fibrillation, non-sustained
atrial fibrillation, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia,
sustained ventricular tachycardia, non-sustained ventricular tachycardia, catecholaminergic
polymorphic ventricular tachycardia (CPVT), heart failure, sudden cardiac death and exercise-
induced sudden cardiac death.

18. (Currently Amended) The method of claim 13, wherein the effective amount of
the agent ~~effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the~~
~~subject is an amount of the agent effective to treat or prevent a cardiac arrhythmia, heart failure,~~
~~and/or exercise-induced sudden cardiac death in the subject.~~ is one or more of:

(a) from about 5 mg/kg/day to about 20 mg/kg/day,

(b) an amount resulting in a plasma concentration of from about 0.02 μ M to about 1.0 μ M
in the subject,

(c) an amount resulting in a plasma concentration of from about 300 ng/ml to about 1000 ng/ml in the subject,

(d) an amount sufficient to increase binding of FKBP12.6 to RyR2 in the subject, or

(e) an amount that is effective to treat or prevent the cardiac condition in the subject.

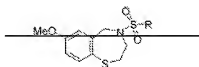
19 – 24. (Cancel)

25. (Currently Amended) The method of claim 13, wherein the agent is S4, S7, S20, S24, S25, S26, S27, or S36.

26. (Original) The method of claim 25, wherein the agent is S36.

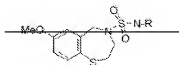
27-28. (Cancel)

29. (Currently Amended) A method for treating or preventing a ~~cardiac arrhythmia, heart failure, and/or exercise induced sudden cardiac death~~ cardiac condition in a subject, comprising administering an effective amount of an agent to the subject, ~~in an amount effective to treat or prevent the cardiac arrhythmia, heart failure, and/or exercise induced sudden cardiac death in the subject,~~ wherein the agent is ~~selected from the group consisting of~~ described by the formula:



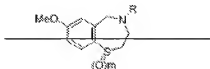
— (a) —

wherein R = aryl, alkenyl, alkyl, $-(CH_2)_nNR'$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



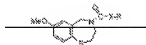
—(b)

wherein R = aryl, alkyl, $(\text{CH}_2)_n\text{NR}'_{25}$, or $(\text{CH}_2)_n\text{SR}'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



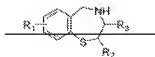
—(e)

wherein R = $\text{CO}(\text{CH}_2)_n\text{XR}'_{25}$, $\text{SO}_2(\text{CH}_2)_n\text{XR}'_{25}$, or $\text{SO}_2\text{NH}(\text{CH}_2)_n\text{XR}'_{25}$, and X = N or S, and n = 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein m = 1 or 2;



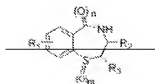
—(d)

wherein R = aryl, alkyl, $(\text{CH}_2)_n\text{R}'_{25}$, $(\text{CH}_2)_n\text{SR}'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein X = NH or O;



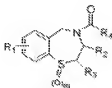
—(e)

wherein R₄ = OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R' = alkyl, aryl, or H; wherein R₂ = H, alkyl, or aryl; and wherein R₃ = H, alkyl, or aryl;



—(f)

wherein R_1 = H, OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R' = alkyl, aryl, or acyl; wherein R_2 = H, alkyl, alkenyl, or aryl; wherein R_3 = H, alkyl, alkenyl, or aryl; wherein m = 0, 1, or 2; and wherein n = 0 or 1;



(g)

wherein R_1 = H, OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R' = alkyl, aryl, or acyl; wherein R_2 = H, alkyl, alkenyl, or aryl; wherein R_3 = H, alkyl, alkenyl, or aryl; wherein R_4 = H, halide, alkenyl, carboxylic acid, or an alkyl containing O, S, or N; and wherein m = 0, 1, or 2; and

~~(h) any or is an~~ oxidized form thereof.

30. (Currently Amended) The method of claim 29, wherein the ~~cardiac arrhythmia is an atrial arrhythmia or a ventricular arrhythmia~~ cardiac condition is selected from the group consisting of cardiac arrhythmia, tachycardia, atrial arrhythmia, atrial tachyarrhythmia, atrial fibrillation, sustained atrial fibrillation, non-sustained atrial fibrillation, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia, sustained ventricular tachycardia, non-sustained ventricular tachycardia, catecholaminergic polymorphic ventricular tachycardia (CPVT), heart failure, sudden cardiac death and exercise-induced sudden cardiac death.

31-32. (Cancel)

33. (Currently Amended) The method of claim 29, wherein the effective amount of ~~the~~ agent effective to treat or prevent a ~~cardiac arrhythmia, heart failure, and/or exercise-induced sudden cardiac death in the subject~~ is one or more of:

(a) from about 5 mg/kg/day to about 20 mg/kg/day,

(b) an amount resulting in a plasma concentration of from about 0.02 μ M to about 1.0 μ M in the subject,

(c) an amount resulting in a plasma concentration of from about 300 ng/ml to about 1000 ng/ml in the subject,

(d) an amount sufficient to increase binding of FKBP12.6 to RyR2 in the subject, or

(e) an amount that is effective to treat or prevent the cardiac condition in the subject.

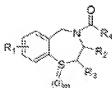
34. (Currently Amended) The method of claim 29, wherein the agent is selected from the group consisting of S4, S7, S20, S24, S25, S26, S27, or and S36.

35. (Original) The method of claim 34, wherein the agent is S36.

36 -42. (Cancel)

43. (New) The method of claim 29, wherein the subject is a human.

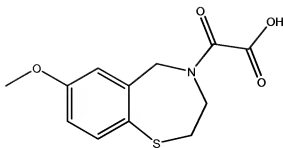
44. (New) A compound having the formula



wherein R_1 = H, OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R' = alkyl, aryl, or acyl; wherein R_2 = H, alkyl, alkenyl, or aryl; wherein R_3 = H, alkyl, alkenyl, or aryl; wherein R_4 = H, halide, alkenyl, carboxylic acid, or an alkyl containing O, S, or N; and wherein m = 0, 1, or 2; or any oxidized form thereof.

45. (New) A compound according to claim 44, wherein the compound is S36 or an oxidized form thereof.

46. (New) A compound having the structure:



or an oxidized form thereof.